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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/434,105	05/03/1995	DAVID A FISCHHOFF	28079/41785	2627

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EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 08/434,105	Applicant(s) FISCHHOFF ET AL.	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2008 and 27 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 47-70, 73 and 77-141 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47-70, 73 and 77-141 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/27/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 47-70, 73 and 77-141 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 47-70, 73 and 77-141 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Dependent claims are included in all rejections. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 20 February 2008, as applied to claims 47-141. Applicant's arguments and the Declaration of Dr. Baum, both filed 20 August 2008, have been fully considered but they are not persuasive.

Previously presented rejections (f) and (h) are withdrawn in light of Applicant's amendment of the claims.

Previously presented rejection (d) is withdrawn in light of Applicant's arguments.

Previously presented rejection (e) is withdrawn in light of Applicant's cancellation of claims 71-72 and 74-76 and arguments with respect to claims 73 and 77.

As Applicant addresses rejections (a) and (g) together, they will be presented together, and Applicant's arguments to both addressed together.

(a) Neither the instant specification nor the originally filed claims appear to provide support for modifying any insecticidal protein coding sequence derived from any *Bacillus* species in claims 47, 51, 63, 112, 113, 117 and 119. Neither the instant specification nor the originally filed claims appear to provide support for the concept of the insecticidal protein coding sequence being from any *Bacillus* species. Nowhere in the specification or the originally filed claims is the starting material from any *Bacillus* species, only *B. thuringiensis*. The specification indicates that insecticidal protein coding sequences only from *Bacillus thuringiensis* were considered (see pg 16, lines 28, to pg 22, line 24, and originally filed claims 3, 9, 13, and 30).

(g) Neither the instant specification nor the originally filed claims appear to provide support for the concept of the starting material being the coding sequence for any insecticidal protein, as in claim 126. The specification indicates that only insecticidal protein coding sequences from *Bacillus thuringiensis* were considered (see pg 16, lines 28, to pg 22, line 24, and originally filed claims 3, 9, 13, and 30).

Applicant urges that the rejection is moot with respect to amended claims 59 and 67 (response pg 23).

This is agreed, and the rejection as it applies to these claims and amended claim 55 is withdrawn.

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Applicant urges and the Declaration states that the inventors state that their invention has broad applicability, and specifically mention plant genes, genes encoding non-plant proteins and genes encoding insecticidal protein from *Bacillus thuringiensis*; it would be clear to a reader that the invention was broader than Bt insecticidal protein coding sequences (response pg 23-24; Declaration ¶3.2-3.4).

This is not found persuasive because it is not clear that the subgenus of *Bacillus* genes was specifically included to the extent it could be claimed. See *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972), which says that a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads.

Applicant urges that one of skill in the art reading the application would not conclude the invention was limited to Bt insecticidal protein genes (response pg 24).

This is not found persuasive because it is not; however, the only insecticidal protein coding sequences for which there is support in the specification are those from *Bacillus thuringiensis*.

Applicant urges that one of skill in the art would have understood that within the broader genus of non-plant protein coding sequences, the invention would be applicable to being applied to protein coding sequences from the genus *Bacillus* (response pg 24-25).

This is not found persuasive because how one of skill in the art could envision the method being applied is not the same for what had support in the specification. There is no support for the claimed subgenus.

Applicant urges and the Declaration states that the Application points to the *Bacillus* genus as being amenable to genetic modification to enhance protein production with respect to

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AT content and codon usage; one of skill in the art would have understood the detrimental sequences could be identified in Bacillus sequences (response pg 25; Declaration ¶3.4-3.10).

This is not found persuasive because the context of pg 21-22 is with respect to expression of Bt genes in plants. That one of skill in the art would have understood the detrimental sequences could be identified in any sequence from any Bacillus species does not mean Applicant has written description support in the specification for claiming applying the method to these sequences.

Applicant urges that identification of a genus and numerous working examples within a species of the genus is sufficient to satisfy written description, citing the MPEP; extensive description of the Bacillus genus was not necessary because bacteriology was an established field (response pg 26-27).

This is not found persuasive because the MPEP uses “genus” and “species” differently than is used in taxonomy. The specification does not indicate that genes from Bacillus species as a whole were contemplated; thus, there is no support for claims to applying the method to them. An extensive description of the Bacillus genus is not required.

Applicant urges and the Declaration states that the specification indicates that the method can be used to prepare genes that encode non-plant proteins, with the example a PLRV coat protein; thus the purpose was expressing proteins in pest resistance (response pg 27-29; Declaration ¶3.11).

This is not found persuasive because the cited pages do not provide support for claims to the subgenus of any insecticidal protein.

The Declaration states that pg 90 discusses expressing two insecticidal proteins in the same plant (Declaration ¶3.12).

This is not found persuasive because the context of pg 90 is with respect to expression of two Bt proteins in plants, specifically, HD1 and HD73.

The Declaration states that Bt insecticidal protein genes were a preferred source, and one of skill in the art would understand that other genes were contemplated; further at the time of filing other *Bacillus* species were known to have insecticidal properties, citing Lysenko et al. Steinkraus et al, Aronson et al, Favret et al, Baumann et al and Bowditch et al (Declaration ¶3.13-3.14).

This is not found persuasive because, as discussed above, most of the genes on the list do not have support in the specification. Just because the art knew of insecticidal proteins from other *Bacillus* species, does not mean that Applicants have support for claiming them. The art does not show that one *Bacillus* strain or protein is synonym of another; thus, the recitation of insecticidal protein coding sequences from any *Bacillus* species or any organism is new matter.

(b) Neither the instant specification nor the originally filed claims appear to provide support for the concept of producing a coding sequence that is devoid or substantially devoid of polyadenylation signal sequences but not devoid or substantially devoid of ATTTA sequences and vice versa, as in claims 63, 67, 112, 114, 117, 126 and 128.

Neither the instant specification nor the originally filed claims appear to provide support for the concept of producing a coding sequence that has a reduction of polyadenylation signal

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sequences but not ATTTA sequences and vice versa, as in claims 47, 51, 55, 59, 113, 119, 120, 122, and 124.

In original claims 13 and 33 the sequences are substantially devoid of both.

Applicant urges and the Declaration states that pg 22-23 of the specification indicate that while substantially all the polyA and ATTTA sequence be removed, enhanced expression is observed with only partial removal of either; this would mean that removal of one but not both is encompassed (response pg 29-30; Declaration ¶4.2-4.3).

This is not found persuasive because in context, this means one is eliminated and the other reduced, not that one is reduced and the other not. Further, it provides no support for one being eliminated and the other not.

Applicant urges and the Declaration states that these sentence means that some of the ATTTAs could be removed, some of the polyAs could be removed, all or substantially all the ATTTAs could be removed, all or substantially all the polyAs could be removed, some of the ATTTAs and polyAs could be removed, or that all the ATTTAs and polyAs could be removed (Declaration ¶4.3-4.4).

This is not found persuasive because there is no support for removing some, all or substantially all the polyAs alone, some, all or substantially all the ATTTAs alone.

Applicant urges and the Declaration states that this is seen in the Examples, where in examples 2 and 3 all or substantially all of one or both are removed or example 1 where some of only one where removed (response pg 32; Declaration ¶4.5).

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This is not found persuasive because in example 1 numerous other bases, not involved in ATTA or polyA sequences, were also changed.

(c) Neither the instant specification nor the originally filed claims appear to provide support for the starting material being sequences encoding portions of any two or more insecticidal polypeptides, as in claims 55 and 67. The only multiple starting sequences originally conceived are specific B.t. insecticidal proteins.

Neither the instant specification nor the originally filed claims appear to provide support for the starting material or protein being hybrids of at least any two B.t. insecticidal proteins or their coding sequences, as in claims 91-92.

Neither the instant specification nor the originally filed claims appear to provide support for the insecticidal protein being any insecticidal fusion, as in claims 113-114.

Applicant urges that Example 3 provides examples of fusions (response pg 21).

This is not found persuasive because the example only provides support for a particular HD1/HD73 fusion; the other fusions were fusions of HD73 synthetic coding sequence with HD73-wild-type coding sequence. The Example does not provide support for fusions involving any protein or other Bacillus insecticidal proteins.

Applicant urges and the Declaration states that one of skill in the art would understand that the inventors contemplated practicing the method on fusion/hybrids of coding sequences from two insecticidal proteins given the representative examples of Bt fusions and the knowledge in the art (response pg 32-33; Declaration ¶5.1-5.3).

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This is not found persuasive because knowledge in the art is not the same thing as support in the specification for claims to use of specific starting materials. There is no mention of the use of the broad genus fusion proteins in the specification; the only mention of fusion protein is with respect to specific B.t. insecticidal fusion proteins. Thus, there is no support for claiming the broad genus.

4. Claims 47-112, 117-118 and 120-141 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

The rejection is modified from the rejection set forth in the Office action mailed 30 May 2007, as applied to claims 47-58 and 63-111. Applicant's arguments filed 30 November 2007 have been fully considered but they are not persuasive.

The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 February 2008, as applied to claims 47-112, 117-118 and 120-141. Applicant's arguments and the Declaration of Cr. Baum, both filed 20 August 2008, have been fully considered but they are not persuasive.

Previously presented rejection (b) is withdrawn in light of Applicant's arguments.

(a) Claims 63-68, 112, 117-118 and 126-129 are indefinite in their recitation of "substantially devoid". "Substantially" is a relative term that renders the claims indefinite - what level of reduction is considered "substantial"?

Applicant urges and the Declaration states that relative terms are common in the art, and readily understood by scientists (response pg 36-37; Declaration ¶8.2).

This is not found persuasive. If the term is readily understood, then Applicant should be able to state what the number is meant by “substantially devoid”; not such number is given. Further, the specification provides no guidelines for the term.

Applicant urges and the Declaration states that the term “substantially devoid” refers to a situation where one or a few problem sequences remain, but the application indicates that removing all is preferable (response pg 37; Declaration ¶8.3).

This is not found persuasive because the upper limit of “a few” is not clear.

Applicant urges and the Declaration states that Example 2 provides an instance where HD-1 was made to have no ATTTA sequences and one polyA sequence, and Example 3 provides an instance in which a fusion was made to have no ATTTA sequences and two polyA sequences (response pg 37; Declaration ¶8.4).

This is not found persuasive because these examples do not define an upper limit on “substantially devoid”. How many polyA or ATTTA sequences can be in the final coding sequence?

Applicant urges and the Declaration states that whether removal of 50% of the sequences constitute “substantially devoid” depends on how many sequences remain - 50 sequences would not be “substantially devoid” (response pg 38; Declaration ¶8.5).

This is not found persuasive. In Example 1, Wild-type HD-1 had only some ATTTA and polyA sequence removed. Is the resulting sequence “substantially devoid” of ATTTA sequences? Would removal of only one of the HD-1 ATTTA sequences constitute “substantially

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devoid”? Was the original sequence “substantially devoid”? What is the upper limit of “substantially devoid”?

(c) Claims 47, 51, 55, 120, 122, and 124 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: making the structural gene comprising a coding sequence that encodes the protein in step (a). As currently written there is no connection between the starting material of part (a) and the making step (c) except the substituted codons - the rest of the codons of the coding sequence of step (a) are not necessarily involved in step (c). A similar disconnect between the steps is seen in claims 59 and 63.

Applicant urges that the claims contain all appropriate connection between the starting material in part (a) and the making step (c); the starting material in claim 47 encodes an insecticidal protein and the encoded protein of part (c) is also insecticidal (response pg 40).

This is not found persuasive. For example, in claim 47, steps (a) and (b) reduce ATTTA or polyA signal sequences in a coding sequence. There is no requirement in step (c) that the structural gene comprise the coding sequence acted on in steps (a) and (b); it only has to have codons that were substituted in (b). Thus, if in (b) all the TTA codons were replaced with TTG, then all the claim requires in step (c) is that any insecticidal protein encoding structural gene have its TTA codons replaced with TTG. There is no requirement that the coding sequence of (a) and (b) have any other relationship to the structural gene of (c). There is not even any requirement in (c) that the structural gene encode an insecticidal protein from *Bacillus*.

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Applicant and the Declaration urge that the specification teaches that the starting material and the modified gene should encode the same protein, but this is not required (response pg 40; Declaration ¶10.1-10.2).

This is not found persuasive because there is no connection between the materials of steps (a) and (b) and that of step (c), as discussed above.

Applicant and the Declaration urge that at the time of filing, scientists were able to make mutations that were not activity destroying (response pg 40; Declaration ¶10.2).

This is not found persuasive because this is not an enablement rejection.

The following rejections are new, due to Applicant's amendment of the claims:

(d) Claims 59-62, 70, 80 lack antecedent basis for the limitation "the wild-type *Bacillus* gene sequence(s)".

(e) Claims 95-96 lack antecedent basis for the limitation "the insecticidal protein derived from *Bacillus*".

Conclusion

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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November 25, 2008

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638